National Human Genome Research Institute (NHGRI)
Patent-Pending Technology Available for Licensing

New Targeted Leukemia Therapy

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Summary

Most acute myeloid leukemia (AML) cases are characterized by specific chromosomal abnormalities and are divided into three major classes based on the disruptions of specific genes: core binding factor (CBF) associated leukemia, mixed lineage leukemia 1 (MLL) associated leukemia, and PML-RARalpha-associated leukemia. Runt-related transcription factor 1 (RUNX1, also known as AML1, a subunit of CBF) plays an essential role in normal hematopoiesis and has been shown to be a tumor suppressor in CBF leukemia. Surprisingly, evidence indicates that RUNX1 activity is also required for growth of AML cells and that inhibition of RUNX1 suppresses leukemia progression.

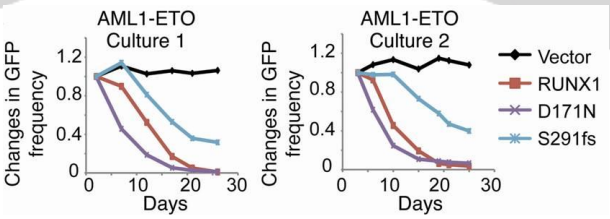
Scientists from the National Human Genome Research Institute (NHGRI) at the National Institutes of Health (NIH) have developed a novel in vitro protein-protein interaction assay and screened a library of approximately 243,000 compounds. A series of compounds have been identified that inhibited the interaction between CBFβ and RUNX1 at the protein level. These compounds also selectively killed CBF leukemia cells in culture, blocked the RUNX1/CBFβ function in zebrafish, and suppressed leukemia progression in mouse models of CBF leukemia.

Potential Commercial Applications

The identified compounds, which include MLS0007661 05, R05-3335, and R024-7429, may be used as a new targeted therapy for the treatment of CBF leukemias as well as a growing number of RUNX and CBFβ related disorders being identified through collaborations.

Related Article

Goyama, S. et al., *Transcription factor RUNX1 promotes survival of acute myeloid leukemia cells* 123(9) J. Clin. Invest. 3876
http://www.jci.org/articles/view/68557



Over expression of RUNX1 or the expression of mutant RUNX1 inhibited the growth of engineered AML cells.